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PATENT
Attorney Docket No.: 015280-290110US
DHHS No.: E-171-96/1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Klimpel *et al.* Application No.: Not yet assigned Filed: May 9, 2001 For: TARGETING ANTIGENS TO THE MHC CLASS I PROCESSING PATHWAY WITH AN ANTHRAX TOXIN FUSION PROTEIN	Examiner: Not yet assigned Art Unit: Not yet assigned PRELIMINARY AMENDMENT

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend the application as follows.

IN THE CLAIMS:

Please amend claims 1-7 as follows.

Please cancel claims 8-28.

Appendix A provides the claims with markings to show changes. All pending claims are provided in Appendix B for the Examiner's convenience.

1. (once amended) A composition capable of inducing an immune response in a mammal to cytotoxic T cell epitopes of a full length protein wherein the composition comprises a unit dose of an anthrax protective antigen and said full length protein bound to an

anthrax protective antigen binding protein, wherein the molar ratio of protective antigen to the full length protein bound to the anthrax protective antigen binding protein is greater than one.

2. (once amended) The composition of claim 1 wherein the protective antigen is a processed protective antigen.

3. (once amended) The composition of claim 1 wherein the composition is sterile.

4. (once amended) The composition of claim 1 wherein the composition further comprises physiologically compatible salts.

5. (once amended) The composition of claim 4 wherein the composition is in an aqueous solution of physiologically compatible salts.

6. (once amended) The composition of claim 1 wherein the anthrax protective antigen binding protein is the lethal factor of *Bacillus anthracis*.

7. (once amended) The composition of claim 1 wherein the anthrax protective antigen binding protein comprises at least about the first 250 amino acid residues of the lethal factor of *Bacillus anthracis* and less than all of the amino acid residues of the lethal factor.

REMARKS

With this amendment, claims 1-7 are pending in the application, and claims 8-28 have been canceled.

1. The invention

The present application relates to methods of using binary bacterial toxins to deliver whole proteins to the cytosolic MHC class I processing pathway. The *Bacillus anthracis* binary toxin is one example of such a binary toxin. This toxin consists of two

proteins: protective antigen ("PA") and lethal factor ("LF"). In this system, PA binds to a cellular receptor, LF binds to PA, and then the binary toxin is translocated into a cell. LF fusion proteins that contain the PA binding domain of LF are also endocytosed into a cell after binding to PA. These fusion proteins are efficiently processed by the cytosolic pathway into epitopes that are presented on MHC class I molecules.

This system therefore surprisingly provides methods of making and administering CTL vaccines, which are processed via the classical MHC class I pathway. The inventors provide for the first time evidence that the binary toxin fusion proteins of the invention are processed by the cytosolic MHC class I pathway and efficiently presented on MHC class I molecules. In particular, the inventors have discovered that this system can be used to accommodate large fusion proteins, thereby providing presentation of multiple epitopes that are recognized by more than one MHC class I allele. CTL vaccines made using the binary toxin system thus can be used to provide broad population coverage for a particular antigen.

2. Status of the claims

Claim 1 has been amended to recite that the antigen is a "full length protein." This amendment add no new matter. Support for these claims can be found, e.g., in the specification on page 3, line 25.

Claim 1 has been amended to recite "cytotoxic T cell" epitopes of the full length protein antigen. This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 1, line 31-32.

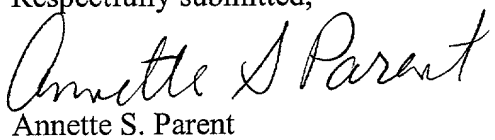
Claim 1 has been amended to recite that the molar ratio of protective antigen to the antigen bound to the anthrax protective antigen binding protein is "greater than one." This amendment adds no new matter. Support for these claims can be found, e.g., in the specification on page 20, line 1.

Claims 1-7 have been amended to recite "composition." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 19, lines 5-7 and lines 29-32.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGE

1. (once amended) A [vaccine] composition capable of inducing an immune response in a mammal to [a specific antigen] cytotoxic T cell epitopes of a full length protein wherein the [vaccine] composition comprises a unit dose of an anthrax protective antigen and said [specific antigen] full length protein bound to an anthrax protective antigen binding protein, wherein the molar ratio of protective antigen to the full length protein bound to the anthrax protective antigen binding protein is greater than one.

2. (once amended) The [vaccine] composition of claim 1 wherein the protective antigen is a processed protective antigen.

3. (once amended) The [vaccine] composition of claim 1 wherein the [vaccine] composition is sterile.

4. (once amended) The [vaccine] composition of claim 1 wherein the [vaccine] composition further comprises physiologically compatible salts.

5. (once amended) The [vaccine] composition of claim 4 wherein the [vaccine] composition is in an aqueous solution of physiologically compatible salts.

6. (once amended) The [vaccine] composition of claim 1 wherein the anthrax protective antigen binding protein is the lethal factor of *Bacillus anthracis*.

7. (once amended) The [vaccine] composition of claim 1 wherein the anthrax protective antigen binding protein comprises at least about the first 250 amino acid residues of the lethal factor of *Bacillus anthracis* and less than all of the amino acid residues of the lethal factor.

APPENDIX B

PENDING CLAIMS

1. (once amended) A composition capable of inducing an immune response in a mammal to cytotoxic T cell epitopes of a full length protein wherein the composition comprises a unit dose of an anthrax protective antigen and said full length protein bound to an anthrax protective antigen binding protein, wherein the molar ratio of protective antigen to the full length protein bound to the anthrax protective antigen binding protein is greater than one.

2. (once amended) The composition of claim 1 wherein the protective antigen is a processed protective antigen.

3. (once amended) The composition of claim 1 wherein the composition is sterile.

4. (once amended) The composition of claim 1 wherein the composition further comprises physiologically compatible salts.

5. (once amended) The composition of claim 4 wherein the composition is in an aqueous solution of physiologically compatible salts.

6. (once amended) The composition of claim 1 wherein the anthrax protective antigen binding protein is the lethal factor of *Bacillus anthracis*.

7. (once amended) The composition of claim 1 wherein the anthrax protective antigen binding protein comprises at least about the first 250 amino acid residues of the lethal factor of *Bacillus anthracis* and less than all of the amino acid residues of the lethal factor.